

PCT

**NOTIFICATION OF THE RECORDING  
OF A CHANGE**

(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

DE CLERCO, Ann  
De Clercq, Brants & Partners cv  
E. Gevaertdreef 10a  
B-9830 Sint-Martens-Latem  
BELGIQUE

Date of mailing (day/month/year)  
22 December 2000 (22.12.00)

Applicant's or agent's file reference  
PCT99.100.AR

**IMPORTANT NOTIFICATION**

International application No.  
PCT/EP99/07065

International filing date (day/month/year)  
22 September 1999 (22.09.99)

1. The following indications appeared on record concerning:

☐ the applicant ☐ the inventor ☒ the agent ☐ the common representative

Name and Address

DE CLERCO, Ann  
Ann De Clercq & Co. B.V.B.A.  
Brandstraat 100  
B-9830 Sint-Martens-Latem  
Belgium

State of Nationality

State of Residence

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+32 9 280 23 40

Facsimile No.

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Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☒ the name ☒ the address ☐ the nationality ☐ the residence

Name and Address

DE CLERCO, Ann  
De Clercq, Brants & Partners cv  
E. Gevaertdreef 10a  
B-9830 Sint-Martens-Latem  
Belgium

State of Nationality

State of Residence

Telephone No.

+32 9 280 23 40

Facsimile No.

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Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned  
☐ the International Searching Authority ☒ the elected Offices concerned  
☒ the International Preliminary Examining Authority ☐ other:

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Authorized officer

Dominique DELMAS

Facsimile No.: (41-22) 740.14.35

Telephone No.: (41-22) 338.83.38

From the INTERNATIONAL BUREAU

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C.20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 04 May 2000 (04.05.00)	
International application No. PCT/EP99/07065	Applicant's or agent's file reference PCT99.100.AR
International filing date (day/month/year) 22 September 1999 (22.09.99)	Priority date (day/month/year) 24 September 1998 (24.09.98)
Applicant JANNES, Geert et al	

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

04 April 2000 (04.04.00)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Claudio Borton Telephone No.: (41-22) 338.83.38
---	--

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>PCT99.100.AR</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/EP 99/ 07065</b>	International filing date (day/month/year) <b>22/09/1999</b>	(Earliest) Priority Date (day/month/year) <b>24/09/1998</b>
Applicant <b>INNOGENETICS N.V. et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

**IDENTIFICATIN OF MIKROOGANISMS CAUSING ACUTE RESPIRATORY TRACT INFECTIONS (ARI)**

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>7</sup> :</b> <b>C12Q 1/68</b>	<b>A1</b>	<b>(11) International Publication Number:</b> <b>WO 00/17391</b> <b>(43) International Publication Date:</b> 30 March 2000 (30.03.00)
<b>(21) International Application Number:</b> PCT/EP99/07065 <b>(22) International Filing Date:</b> 22 September 1999 (22.09.99)  <b>(30) Priority Data:</b> 98870203.1 24 September 1998 (24.09.98) EP  <b>(71) Applicant (for all designated States except US):</b> INNOGENETICS N.V. [BE/BE]; Industriepark Zwijnaarde 7, Box 4, B-9052 Ghent (BE).  <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> JANNES, Geert [BE/BE]; E. Vanhoorenbekelaan 23/1, B-3010 Leuven (BE). SCHMITT, Heinz-Josef [DE/DE]; Poggenkaugsweg 1a, D-24113 Molssee (DE).  <b>(74) Agent:</b> DE CLERCQ, Ann; Ann De Clercq & Co. B.V.B.A., Brandstraat 100, B-9830 Sint-Martens-Latem (BE).		<b>(81) Designated States:</b> AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
<b>(54) Title:</b> IDENTIFICATION OF MICROORGANISMS CAUSING ACUTE RESPIRATORY TRACT INFECTIONS (ARI)		
<b>(57) Abstract</b> <p>The present invention relates to a method for the detection of acute respiratory tract infection (ARI) comprising the simultaneous amplification of several target nucleotide sequences present in a biological sample by means of a primer mixture comprising at least one primer set from each one of the following gene regions: the F1 subunit of the fusion glycoprotein gene for RSV, the hemagglutininneuraminidase gene for PIV-1, the 5' noncoding region of the PIV-3 fusion protein gene, 16 S rRNA sequence for <i>M.pneumoniae</i>, 16 S rRNA sequence for <i>C.pneumoniae</i>, the 5' noncoding region for enterovirus, the non-structural protein gene from influenza A, the non-structural protein gene from influenza B, and the hexon gene for adenoviruses. This multiplex RT-PCR method is particularly preferred because it allows to determine the presence of the following microorganisms which infect the respiratory tract of mainly children in one amplification step: RSV, parainfluenza virus, <i>M.pneumoniae</i>, <i>C.pneumoniae</i>, enterovirus, influenza A and B and adenoviruses. The present invention also relates to a kit for performing the above-mentioned detection method as well as to the individual probes and primers used therein.</p>		

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
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EE	Estonia	LR	Liberia	SG	Singapore		

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 99/07065

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>MONTO A S ET AL: "Acute respiratory infections (ARI) in children: prospects for prevention" VACCINE, vol. 16, no. 16, October 1998 (1998-10), page 1582-1588 XP004129212 the whole document</p> <p style="text-align: center;">---</p>	1-10
Y	<p>SAIKKU P: "Atypical respiratory pathogens" CLINICAL MICROBIOLOGY AND INFECTION, vol. 3, no. 6, December 1997 (1997-12), pages 599-604, XP002098063 cited in the application table 1</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p>	1-10

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

17 February 2000

Date of mailing of the international search report

29/02/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Osborne, H

# INTERNATIONAL SEARCH REPORT

International Application No.

PCT/EP 99/07065

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	GILBERT L ET AL: "Diagnosis of viral respiratory tract infections in children by using a reverse transcription-PCR Panel" JOURNAL OF CLINICAL MICROBIOLOGY, vol. 34, no. 1, January 1996 (1996-01), pages 140-3, XP002098027 cited in the application the whole document	1-10
Y	TROLLFORS B ET AL: "Childhood pneumonia: possibilities for aetiological diagnosis" BAILLIERE'S CLINICAL PEDIATRICS, vol. 5, 1997, pages 71-84, XP002098033 cited in the application the whole document	1-10
A	EP 0 576 743 A (AMOCO CORP) 5 January 1994 (1994-01-05) page 1, line 10 - line 18	1-10
Y	WO 98 11259 A (LUINSTRA KATHLEEN ;CHERNESKY MAX (CA); CHONG SYLVIA (CA); DUNN JAM) 19 March 1998 (1998-03-19) the whole document	1-10
Y	ECHEVARRIA J ET AL: "Simultaneous detection and identification of human parainfluenza viruses 1,2 and 3 from clinical samples by multiplex PCR." JOURNAL OF CLINICAL MICROBIOLOGY, vol. 36, no. 5, May 1998 (1998-05), page 1138-91 XP000876835 the whole document	1-10
X	EMBL Database Entry Q06252 Accession Number Q06252: 31 Jan 1991 University Patents INC."Probes for detecting picornavirus." XP002098007 100% identity in 21bp overlap with Seq ID No 4, of table 4	6,7
X	EMBL database entry T10170 Accession Number T10170, 24 July 1996 Mitsubishi Yuka BCL KK. "Adenovirus 3' primer binds to bases 2842-2861." XP002098008 see adenol, table 3.	6,7
P,X	DE 197 16 456 A (SCHMITT HEINZ JOSEF PROF DR) 22 October 1998 (1998-10-22) the whole document	1-10

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 99/07065

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0576743 A	05-01-1994	DE 69215863 D DE 69215863 T	23-01-1997 26-06-1997
WO 9811259 A	19-03-1998	AU 4196297 A	02-04-1998
DE 19716456 A	22-10-1998	NONE	



REC'D 20 DEC 2000

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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference INN-100-PCT/ADC	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP99/07065	International filing date (day/month/year) 22/09/1999	Priority date (day/month/year) 24/09/1998
International Patent Classification (IPC) or national classification and IPC C12Q1/68		
Applicant INNOGENETICS N.V. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 9 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand  04/04/2000	Date of completion of this report  18.12.2000
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Thumb, W  Telephone No. +49 89 2399 7350 

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/07065

## I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:

### Description, pages:

1-33 as originally filed

### Claims, No.:

1-12 as originally filed

### Drawings, sheets:

1/4-4/4 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/07065

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

## IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.  
☐ paid additional fees.  
☐ paid additional fees under protest.  
☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.  
☒ not complied with for the following reasons:  
**see separate sheet**

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☐ all parts.  
☒ the parts relating to claims Nos. 1-5, 8.

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-5, 8
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-5, 8
	No:	Claims	

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP99/07065

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Industrial applicability (IA)    Yes:    Claims    1-5, 8  
   No:    Claims

2. Citations and explanations  
    **see separate sheet**

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:  
**see separate sheet**

**Re Item I**

**Basis of the opinion**

Sequence listing pages 1-9 filed with the letter of 12.1.2000 do not form part of the application (Rule 13<sup>ter</sup>.1(f) PCT).

**Re Item IV**

**Lack of unity of invention**

The application lacks unity within the meaning of Rule 13.1 PCT for the following reasons:

- (a) Claims 1-5 and 8 refer to a multiplex method and a kit, respectively, to simultaneously detect pathogens associated with respiratory tract infections. The method is characterized by the use of a primer mix comprising at least nine different primer sets, said primers being derived from several different microorganisms.
- (b) Claims 6 and 7 refer to individual primers or probes respectively. Even though the sequences of the primers and probes of claims 6 and 7 are related to the microorganisms to be detected by the methods of claims 1-5, the individual primers or probes per se are neither related to the method of claims 1-5, nor to each other, in a way as to form a single general inventive concept.
- (c) Claims 9 and 10 refer to a kit for the detection of acute respiratory tract infection, comprising a set of probes according to claim 5. However, no primers to perform the method of claims 1-4, to which claim 5 refers, are included in the kit of claims 9 and 10, and therefore said kit is not suitable to perform a multiplex method for simultaneous detection of several pathogens by amplification using a primer mix.
- (d) Claim 11 refers to a kit, comprising at least one, meaning one *or* more, primers. Since a kit with one primer is not suitable for performing a method using the amplification of several different targets, the kit of claim 11 is not linked to the inventive concept of claims 1-5 and 8.
- (e) Claim 12 refers to a kit, comprising at least one, meaning one *or* more, nucleic acid probes. Since a kit with one probe is not suitable for performing a method using the amplification of several different targets, the kit of claim 11 is not linked

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/EP99/07065

to the inventive concept of claims 1-5 and 8.

Hence it is considered that the following separate inventions or groups of inventions are not so linked as to form a single general inventive concept:

1. Claims 1-5, 8
2. Claim 6 partially (SEQ ID 17-19, derived from M. pneumoniae)
3. Claim 6 partially (SEQ ID 20,21, derived from C. pneumoniae)
4. Claim 6 partially (SEQ ID 22,23, derived from B. pertussis)
5. Claim 7 partially (SEQ ID 24-26, derived from M. pneumoniae)
6. Claim 7 partially (SEQ ID 27,28, derived from C. pneumoniae)
7. Claim 7 partially (SEQ ID 29,30, derived from B. pertussis)
8. Claim 7 partially (SEQ ID 31, derived from RSV6)
9. Claim 7 partially (SEQ ID 32, derived from RSV7)
10. Claim 7 partially (SEQ ID 33, derived from RSV8)
11. Claim 7 partially (SEQ ID 34, derived from RSV9)
12. Claim 7 partially (SEQ ID 5, derived from Influenza A)
13. Claim 7 partially (SEQ ID 6, derived from Influenza B)
14. Claim 7 partially (SEQ ID 7-9, derived from Adenovirus)
15. Claim 7 partially (SEQ ID 10-12, derived from Parainfluenza 1)
16. Claim 7 partially (SEQ ID 13, derived from Parainfluenza 3)
17. Claim 7 partially (SEQ ID 14, derived from RSV)
18. Claim 7 partially (SEQ ID 15, derived from M. pneumoniae)
19. Claim 7 partially (SEQ ID 16, derived from C. pneumoniae)
20. Claims 9-10
21. Claim 11
22. Claim 12

**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Since the applicant did not respond to the invitation to restrict the present application or to pay additional fees, sent with the letter dated 2.6.2000, the

international preliminary examination report is established on those parts which in the opinion of this Authority appears to relate to the main invention, i.e. claims 1-5 and 8 (Article 34(3)c) PCT).

2. Reference is made to the following documents:

D1: ECHEVARRIA J ET AL: 'Simultaneous detection and identification of human parainfluenza viruses 1,2 and 3 from clinical samples by multiplex PCR.'  
JOURNAL OF CLINICAL MICROBIOLOGY, vol. 36, no. 5, May 1998 (1998),  
page 1138-91.

D2: SAIKKU P: 'Atypical respiratory pathogens' CLINICAL MICROBIOLOGY  
AND INFECTION, vol. 3, no. 6 (1997), pages 599-604.

3. Novelty

3.1 Independent claim 1 is novel in the sense of Article 33(2) PCT since a method for detection of acute respiratory tract infection comprising the simultaneous amplification of 9 target nucleic acids using a primer mixture does not form part of the known prior art.

3.2 The same applies to dependent claims 2-5, and claim 8, the latter referring to a kit to perform the method of claims 1-4.  
Claims 2-5 and 8 therefore also meet the requirements of Article 33(2) PCT.

4. Inventive step

4.1 Document D1, which is considered to represent the most relevant state of the art referring to claim 1, discloses the simultaneous detection of different serotypes of human parainfluenza viruses (HPIV) using multiplex reverse transcription (RT)-PCR (page 1388, Abstract, lines 3-4). Primers were derived from sequences of the hemagglutinin-neuraminidase gene of HPIV (page 1388, col. 2, lines 29-35). PCR products of an expected size, depending on the selected primers, were obtained with three HPIV prototype strains when they were tested alone or in a

mixed reaction (page 1389, col. 2, lines 20-22; page 1390, figure 1).

The subject-matter of claim 1 differs from the teaching of D1 in that a method is disclosed using a primer mixture, consisting of at least 9 primer pairs, and wherein said primers are derived from specific regions of 9 different microorganisms causing respiratory tract infection.

The underlying problem is therefore considered as to provide a method to simultaneously detect a combination of a larger number of different pathogens causing respiratory tract infections.

Document D2 discloses a number of pathogens related with atypical pneumonia. Microorganisms are included, which provide target nucleic acid sequences of present claim 1 (page 599, col. 2, table 1).

However, even though the target sequences, which can be used to specifically detect the pathogens comprised in claim 1 (see references in the description, page 13, lines 21-25) are known, it would not be obvious for the person skilled in the art to combine said specific sequences in one multiplex RT-PCR reaction to arrive at the solution to the above stated problem.

Claim 1 therefore meets the requirements of Article 33(3) PCT.

- 4.2 The same applies to dependent claims 2-5, which thus are also inventive in the sense of Article 33(3) PCT.
- 4.3 Claim 8, referring to a kit for performing the method of claims 1-4 meets the requirements of Article 33(3). It is considered that as soon as a method is inventive, a kit assembled to perform said method is also inventive.
- 5. The document DE-A-197 16 456 indicated in the international search report as an intermediate document is not to be regarded as state of the art according to Article 33(2) PCT, as the date of priority claimed can be allowed for the relevant parts of the present application.

#### **Re Item VII**

#### **Certain defects in the international application**

References "incorporated herein by reference" (page 9, lines 2-3) should be deleted as



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the application should disclose the invention in a manner sufficiently complete for it to be carried out by a person skilled in the art (Article 5 PCT).